

Sleep Deprivation Impairs Memory by Altering Cofilin and Actin Signaling

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Sleep deprivation is a significant public health issue affecting millions of people. Insufficient sleep attenuates brain function, particularly targeting the hippocampus, and contributing to cognitive disorders and psychiatric diseases. However, the molecular mechanisms by which sleep deprivation impairs memory storage are not defined. We show that sleep deprivation alters hippocampal actin dynamics through increased activity of the filamentous actin-severing enzyme cofilin. Viral expression of inactive mutant cofilin selectively in hippocampal excitatory neurons makes memory consolidation resistant to sleep loss. The sleep deprivation-induced increase in cofilin activity and associated memory deficits are prevented by increasing cAMP levels or suppressing PDE4A5 function using novel pharmacogenetic and viral approaches. Transient sleep loss alters molecular signaling cascades within hippocampal neurons, leading to changes in actin dynamics and impairments in memory storage.

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